European Federation of Pharmaceutical Industries and Associations

## EFPIA/VE Final Response to DG Sante Call for Evidence on Revision of EU Variations Framework

EFPIA/Vaccines Europe (VE) fully support the need to revise the EU variations framework. We believe such a revision must be extensive and enable a science- and risk-based approach to lifecycle management, allowing the future framework to keep pace with innovation and ensure a sustainable supply of medicines throughout the product lifecycle. We believe that despite the constraints of the current pharmaceutical legislation, significant progress can be made in the next 12 months and we encourage the EC to keep the broader goal in mind when considering all changes needed. More details are included in the Annex but the immediate priorities are: 1) Apply the same principles to change categorization (science-and risk-based) to all technologies including biologicals, vaccines, ATMPs, drug-device combinations, and IVDs. 2) Remove from Annex II of Reg 1234/2008 items *2(e)* "*variations related to modifications in the manufacturing process or sites of the active substance for a biological medicinal product*" and *2(f)* "*variations related to the introduction of a new design space or the extension of an approved one."* 3) Apply risk-based approaches to the submission of variations that have an impact on the Product Information. 4) Accommodate innovation, emerging science and sustainability through classifications which consider ICHQ12 tools and principles in the following way: allow a flexible/expanded use of Post Approval Change Management Protocols (PACMPs), and other structured protocol-driven changes; remove default Type IB classification for biologicals and immunologicals from B.I.e.5(c) and B.II.g.5(c) (2013/C 223/01); facilitate multi-product protocols to support changes across similar product types and use of existing grouping and worksharing procedures for change; ensure the flexible use of PACMPs to enable proposing all types of change, including those affecting multiple sites/products to be managed under a company pharmaceutical quality system (PQS) with no regulatory submission; include Established Conditions and Product Lifecycle Management as per ICHQ12 (in 2013/C 223/01) and utilize the regulatory sandbox concept to gain greater understanding of these new tools. 5) Expand the EU Masterfile system (within the general pharmaceutical legislation) to include the option of a Platform Technology Master File (PTMF) and revise the Variation framework to fully enable an efficient lifecycle management of any new types of master file. 6) Adopt new technologies, such as model-based process controls, allowing the management of changes to control variables as notifications or under the PQS, where justified (aligned with the planned revisions of EMA/CHMP/QWP/63699/2014). 7) Expand the use of existing IT solutions to maintain administrative information associated with the Marketing Authorisation, thereby removing the requirement to submit minor changes for review whilst evaluating advances in cloud-based technology to enable real-time oversight of the dossier by regulators. 8) Include accelerated assessment procedures and timelines for variations associated with major public health interest or significant therapeutic innovation e.g., new indication. 9) Refine and expand existing concepts such as work-sharing procedures and grouping to reduce time for review/approval of the change and its implementation, especially where the same change affects multiple products and procedures. 10) Consider including the concept of worksharing and regulatory reliance/alignment with other regulatory agencies outside the EU.

EFPIA/VE believe a comprehensive revision of the variation framework is necessary to realise the potential for a streamlined, future-proof framework. To enable success, there needs to be full commitment and collaboration to undertake all necessary revisions in the context of both the current and future legislative framework for medicines in a timely manner. We will continue to do all we can to advance this topic with all stakeholders.